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Predictive and Prognostic Role of P53 According to Tumor Phenotype in Breast Cancer Patients Treated with Preoperative Chemotherapy: A Single-Institution Analysis

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Valentina Guarneri, Elena Barbieri, Federico Piacentini, ...

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Abstract

Introduction and aims

The p53 protein is a mediator of the cellular response to DNA damage. The aim of this study was to evaluate the predictive and/or prognostic value of p53 expression in relation to the molecular subtypes of breast cancer in patients treated with preoperative chemotherapy.

Patients and methods

Patients with stage II-III breast cancer were included in the study. The expression of p53 was evaluated by immunohistochemistry on the diagnostic core biopsy specimen. Patients received 4–6 courses of preoperative chemotherapy. Pathological complete response (pCR) was defined as complete disappearance of invasive tumor in the breast and axillary lymph nodes.

Results

154 patients were included in the study and the molecular subtypes of their tumors were classified as follows: triple negative 18.2%, hormone receptor positive 60.4%, and HER2 positive 21.4%. p53 was expressed in 43.5% of the patients. A significant association between p53 expression and breast cancer molecular subtypes, tumor differentiation, and proliferation was observed. pCR was achieved in 8 patients (5.2%). p53 expression, molecular subtype, and nuclear grading were significant predictors of pCR (odds ratio for pCR in patients with p53-expressing tumors 10.03, p=0.0077). In univariate analysis, the expression of p53 as well as high proliferation and lymph node involvement after preoperative chemotherapy were predictors of a worse disease-free survival. Patients with p53 positivity also had a worse overall survival. In multivariate analysis, both p53

expression and nodal status after preoperative chemotherapy were significantly associated with disease-free and overall survival: the hazard ratios for relapse and death in patients with p53-expressing versus non-p53-expressing tumors were 2.29 (p=0.015) and 7.74 (p=0.002), respectively. The hazard ratios for relapse and death in node-positive versus node-negative patients were 3.63 (p=0.003) and 3.64 (p=0.041), respectively.

Conclusions

In this series of patients, p53 expression was significantly associated with markers of aggressive tumor biology, and with a higher likelihood of attaining pCR. p53 expression was a negative prognostic parameter for disease-free and overall survival in univariate and multivariate analysis.

Keywords Breast cancer, Primary systemic therapy, Neoadjuvant chemotherapy, p53, Ki-67, Tumor biomarkers, Predictive factors, Prognostic factors